

In the Specification

Please replace the paragraph beginning at page 3, line 16 and ending at page 3, line 26 with the following paragraph.

International patent application serial number PCT/US00/01997, filed 01/25/00 by Bamdad et al., entitled "Rapid and Sensitive Detection of Aberrant Protein Aggregation in Neurodegenerative Diseases" (published as WO 00/43791 on 07/27/00), International patent application serial number PCT/US00/01504, filed 01/21/00 by Bamdad, et al, entitled "Interaction of Colloid-Immobilized Species with Species on Non-Colloidal Structures" (published as ~~WO 00/34783~~ WO 00/43783 on 07/27/00), commonly-owned, copending U.S. patent application serial no. 09/602,778, filed 06/23/00 by Bamdad et al., entitled "Interaction of Colloid-Immobilized Species with Species on Non-Colloidal Structures"; and commonly-owned, copending U.S. patent application serial no. 09/631,818, filed 08/03/00 by Bamdad et al., entitled "Rapid and Sensitive Detection of Protein Aggregation" all are incorporated herein by reference.

Please replace the paragraph beginning at page 15, line 27 and ending at page 16, line 20, with the following paragraph.

Binding partners 28 can be immobilized relative to colloid particles 30 via thiol linkage. That is, binding partners 28 can incorporate a thiol, or can be chemically attached or otherwise immobilized to a thiol, which will bind to a gold surface of colloid particles 30. In one preferred embodiment proteins 28 are attached to self-assembled monolayers (SAMs) formed on surfaces of gold colloid particles 30 via a metal binding tag/metal/chelate linkage. In such a case a metal binding tag can be attached to binding partner 28, and the colloid can carry a SAM presenting a chelate coordinating a metal to which the binding tag binds. Other affinity tags can be used to attach binding partners 28 to SAM species on the colloid particles. In another embodiment SAMs on colloid particles present carboxylate groups, and binding partners 28 incorporate or are immobilized relative to primary amines which can be linked to the SAMs via EDC/NHS chemistry. Affinity tag/binding partner linkage, or EDC/NHS chemistry can be used to link

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essentially any species to essentially surface of the invention. Preferably such SAMs include sufficient exposure of protein 28 to facilitate binding to drug candidate 24, the remainder of the self-assembled monolayer comprising non-specific binding-inhibiting species such as polyethylene-glycol-terminated SAM-forming species. The selective attachment of various species to self-assembled monolayer-forming species, to form self-assembled monolayers at surfaces exposing desired chemical or biochemical functionality, are known from references noted above and additional documents including U.S. Patent No. 5,512,131 and International Patent Publication WO 96/29629, published June 26, 1996, each of which is incorporated herein by reference. Chemistry for attachment of proteins 28 to colloid particles 38 also is described in co-pending, commonly owned International Patent Application Serial No. PCT/US00/01504 of Bamdad and Bamdad, filed January 21, 2000, published as ~~WO 00/34783~~ WO 00/43783 on 7/27/00 and incorporated herein by reference.